Kidney International, Vol. 60 (2001), pp. 2021–2024

TECHNICAL NOTE

A simple method to estimate the required dialysis time for cases of alcohol poisoning

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A simple method to estimate the required dialysis time for cases of alcohol poisoning.

Background. Conventional dialysis management of ethylene glycol and methanol poisoning includes frequent intradialytic determinations of serum toxin concentration. Dialysis is continued until a target toxin concentration is reached. Initially, the required dialysis duration is unknown, making planning difficult. We devised a simple method to estimate the duration of dialysis required and avoid quantitation of multiple toxin samples.

Methods. Using the assumption that toxic alcohols would have a dialysis clearance similar to urea, we proposed that required dialysis time (hours) to reach a 5 mmol/L toxin concentration target would be: $[-V \ln(5/A)]/0.06k$, where V (liters) is the Watson estimate of total body water, A is the initial toxin concentration (mmol/L), and k is 80% of the manufacturer-specified dialyzer urea clearance (mL/min) at the initial observed blood flow rate. Directly measured dialysis and renal toxin clearance, and true dialysis requirement by conventional treatment protocol were compared with our estimate in two methanol and three ethylene glycol poisonings treated with Fresenius F8 dialyzers.

Results. There were no clinically or statistically significant differences between predicted dialysis duration (7.6 ± 1.9 hours, ±SD) and that actually provided using hourly toxin concentration sampling (7.4 ± 1.9 hours). Renal toxin clearance was negligible compared to that of dialysis, and predicted dialysis clearance did not differ significantly from that observed.

Conclusions. The simple estimate method is sufficiently valid to guide the prescription of dialysis for toxic alcohol poisoning. Data required at dialysis start include only the initial toxin concentration, dialyzer manufacturer's specified urea clearance at initial observed blood pump speed, and patient demographics to estimate total body water. This approach allows for planned dialysis therapy, without the need for additional toxin concentration measurements until dialysis is completed.

Key words: hemodialysis, ethylene glycol, methanol, renal toxicity.

Received for publication March 22, 2001
and in revised form June 1, 2001
Accepted for publication June 5, 2001

Patients poisoned with methanol or ethylene glycol often require prolonged dialysis to achieve a reduction of toxin and metabolites to acceptable levels. Traditional monitoring of this process involves frequent laboratory determinations of these blood concentrations, generating significant labor costs for the laboratory. Such dialyses cause planning difficulties for dialysis nursing staff, since the duration of required dialysis is not usually known at the start of treatment.

We have devised a simple method to estimate required dialysis time for cases of alcohol poisoning. This approach depends on knowing only the toxin concentration at the beginning of the dialysis treatment and the blood flow rate at the initiation of therapy. The remaining parameters are estimated from the manufacturer's dialyzer specifications and the patient's sex, age, height, and weight. This method yields an estimate of required dialysis time sufficiently accurate to eliminate the need for intradialytic blood testing while allowing treatment planning.

METHODS

Patient population

Sequential cases of methanol- or ethylene glycol-poisoned patients receiving dialysis (toxin or metabolite concentration of at least 15 mmol/L) were selected for this study. Five cases were studied between June 2000 and March 2001.

Study protocol

All patients were treated using our pre-existing protocol, which was not altered except for obtaining the urine and dialysate collection as noted later in this article to allow later determination of dialysis and renal clearance of toxins. The observations made for this study did not bias the usual treatment approach at our institution, and all calculations and estimates of required dialysis times were made after the fact by an independent observer not responsible for the patient's care.

In our institution, methanol- or ethylene glycol-poi-

soned patients receiving dialysis were treated as follows: An ethanol intravenous infusion was used to block toxic alcohol metabolism once the diagnosis is suspected, with a target ethanol serum concentration of 22 to 45 mmol/L. During dialysis, this alcohol infusion was continued at the pre-existing rate, and ethanol was added to the dialysate bicarbonate concentrate to achieve a concentration of 33 mmol/L. Since the bicarbonate concentrate (mixed from powder just prior to use) was diluted 1:20 by the dialysis machine, this required the addition of 300 mL of absolute ethanol to each 10 L jug of bicarbonate concentrate. Over many years we have observed that this approach achieves stable blood ethanol concentrations in the target range, so that no adjustment of infusion rates or monitoring of serum ethanol concentrations is needed during dialysis (abstract; Ghabashi, *J Am Soc Nephrol* 11:129A, 2000).

Acute hemodialysis was then initiated via a 20 cm femoral dialysis catheter (Vas-Cath, Mississauga, Ontario, Canada) using a Fresenius F8 dialyzer (Fresenius Medical Care, Toronto, Canada). Blood pump speed was maintained at the maximum obtainable rate, and dialysate flow rate was 500 mL/min. Patients generally were given 1500 units of heparin initially, followed by 500 to 1000 U/hour. Hourly blood concentrations of methanol and formic acid or ethylene glycol and glycolic acid were obtained, and dialysis was continued until a concentration $\leq$8 mmol/L (maximum of methanol or formic acid) or $\leq$6 mmol/L (maximum of ethylene glycol or glycolic acid) was achieved, at which time dialysis was discontinued. Following dialysis the ethanol drip and toxin level monitoring continued until toxin levels fell to $<$5 mmol/L.

Additional determinations for this study included obtaining a 30-minute urine collection between minutes 45 and 75 of dialysis, and a ten-minute dialysate collection from the machine drain line between minutes 55 and 65 of dialysis. Concentrations of toxin and metabolite were measured in urine and dialysate collections, and using the one-hour serum concentration, renal and dialysis clearances of toxin were calculated.

Methanol and formic acid concentrations were analyzed by capillary gas chromatography by a modification of a previously reported method [1]. Ethylene glycol and glycolic acid were analyzed by capillary gas chromatography [2].

Estimate formula

For estimating required dialysis time, we took a simple approach, targeting a toxin level of 5 mmol/L to allow a safety margin from our protocol targets of 6 to 8 mmol/L as noted previously in this article. We assumed that renal clearance and metabolism of toxins were negligible compared with dialysis clearance, that the volume of distribution of toxin was the total body water as determined by the Watson formula [3], and that the dialysis clearance of toxin would be similar to that of urea. To allow estimates to be made at the start of dialysis, we further assumed that toxin clearance during the dialysis would be a constant 80% of the manufacturer's stated urea clearance for the dialyzer at the observed blood pump speed at the initiation of the dialysis run [4]. If the observed blood pump speed was between rates stated in dialyzer specifications, then linear interpolation was used to estimate the appropriate urea clearance. Thus, our estimate requires only data easily determined at the start of dialysis, allowing a slight delay for the initial toxin level to be reported from the laboratory. The larger value of either toxin (methanol/ethylene glycol) or metabolite (formic acid/glycolic acid) was elected as the starting value for the estimate.

Using the previously mentioned assumptions, it is apparent that at time T, the predicted serum toxin concentration P will be as follows:

$$P = Ae^{-(kT/V)} \qquad \text{[Eq. 1]}$$

where A is the initial toxin concentration, k is 80% of the manufacturer's specified urea clearance at the observed blood pump speed, and V is the Watson estimate of total body water. It is then simple to derive an estimate of dialysis time in hours to reach the target concentration of 5 mmol/L:

$$\text{Time estimate} = \frac{-V \ln(5/A)}{0.06k} \qquad \text{[Eq. 2]}$$

where V is liters, Time is hours, A is mmol/L, and k is mL/min.

Analysis

For each treated case, the time estimate (equation 2) was compared with the actual dialysis time as mandated by our pre-existing protocol. In addition, a comparison was made between predicted and measured dialysis toxin clearance, and plots were made of observed versus predicted serum toxin concentrations, using equation 1. Chi-squared tests were used for statistical comparisons. Given the small number of cases, no attempt was made to determine the risk of beta error.

RESULTS

Five patients were included in this study, all of whom survived.

Figure 1 presents the observed and predicted blood toxin concentrations for the five cases examined. The predicted serum toxin concentrations during dialysis using equation 1 were very close to the observed values.

Table 1 presents the predicted and observed dialysis toxin clearances, estimated (equation 2) and required dialysis durations, and observed renal toxin clearances. There were no statistical differences between observed

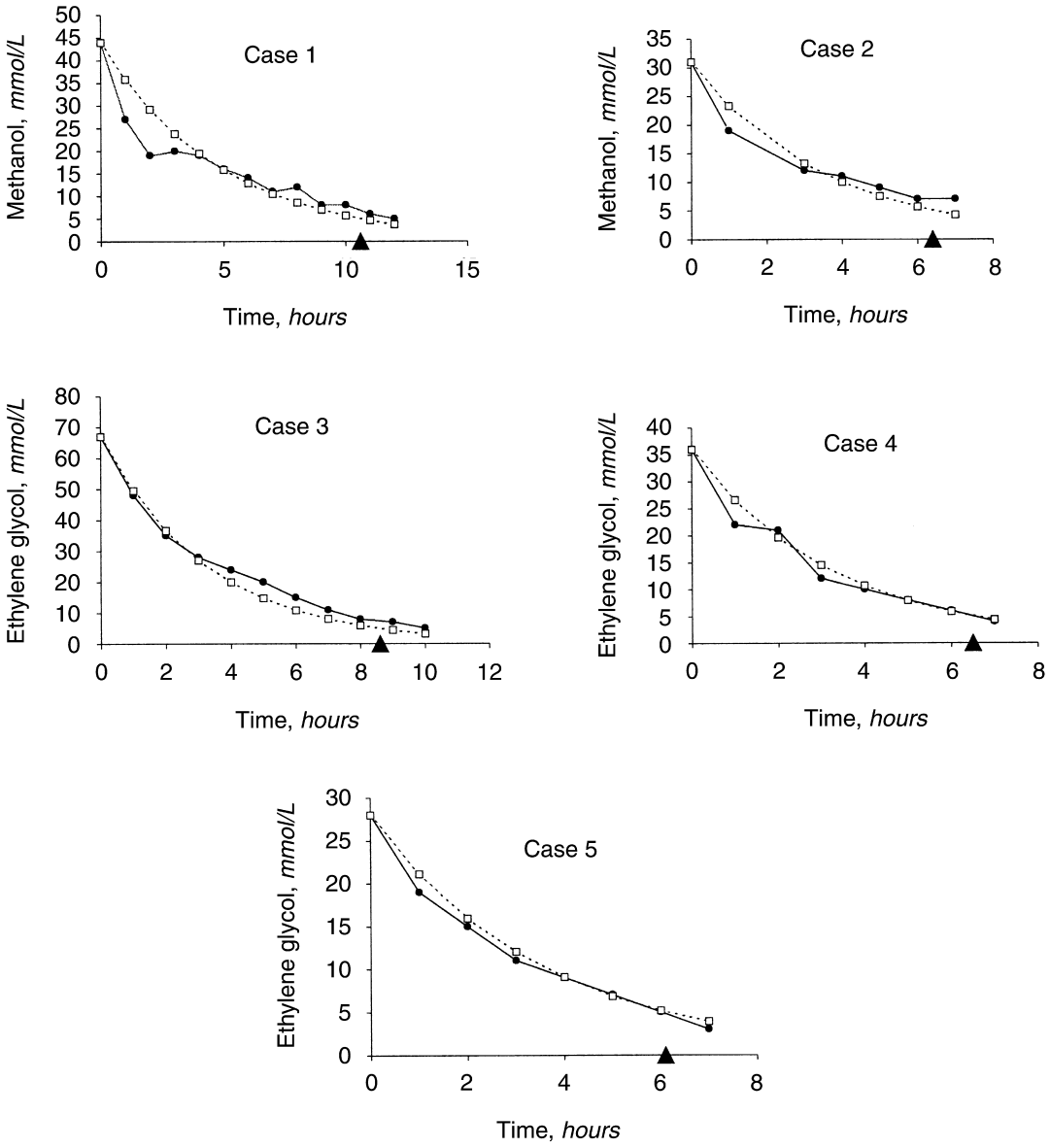

Fig. 1. Methanol or ethylene glycol serum concentration over the elapsed dialysis time in each case studied. Symbols are (●) observed values; (□) concentrations predicted by equation 1; (▲) on the horizontal axes denote the time at which dialysis would be stopped if equation 2 were used to guide therapy.

Table 1. Predicted and observed dialysis data

Case no.	Toxin	Predicted	Observed[a]	Estimated	Required[b]	Renal toxin clearance
		dialysis toxin clearance *L/h*		duration of dialysis *hours*		*L/h*
1	Methanol	10.2	10.0	10.6	9	0.13
2	Methanol	11.5	10.9	6.4	6	0.22
3	Ethylene glycol	9.9	8.5	8.6	10	0.21
4	Ethylene glycol	8.9	9.5	6.5	6	0.12
5	Ethylene glycol	11.7	11.1	6.1	6	0.02

[a] $P > 0.05$ by chi-squared comparison with predicted values
[b] $P > 0.05$ by chi-squared comparison with estimated values

and predicted dialysis clearances or estimated and required dialysis durations. Renal clearances were negligible compared with dialysis clearance of toxins.

DISCUSSION

These data confirm that our simple method of estimating required dialysis duration for toxin removal (equation 2) provides a satisfactory clinical approach. Termination of dialysis at the time point when equation 2 predicts that blood toxin concentration would have reached 5 mmol/L (Fig. 1) would have achieved actual serum toxin concentrations of less than 7 mmol/L in all cases. If a single one- or two-hour post-dialysis blood level is then determined, while the ethanol infusions are continued, ample confirmation of a successful clinical result could be achieved with a considerable saving of laboratory resources. In the rare circumstance where the prediction was inaccurate or significant post-dialysis rebound of toxin concentration occurred, dialysis therapy could be re-initiated. No such rebound was observed in these patients. Obviously, a major reduction in achieved blood pump speed during the dialysis should trigger a re-evaluation of planned dialysis time, but such changes were not observed in the cases studied for this report.

We have only evaluated this method for Fresenius F8 dialyzers. Jindal and Goldstein found that using 80% of the manufacturer's specified urea clearance as an estimate of in vivo urea clearance was valid for two other dialyzers [4], so it is likely that this method of estimating dialysis time for poisonings is applicable to other dialyzers. Any dialysis center planning to use this approach would be well advised to validate this estimate approach for their preferred dialyzers.

This approach would limit the need for toxin concentration measurements to predialysis and postdialysis samples. Given that poisoning patients often present at night, this would significantly reduce the laboratory overtime requirements. Soon after initiating hemodialysis, the physician could estimate the required duration of therapy, allowing improved planning of dialysis nursing coverage.

Although Berendt et al suggested a similar approach, their method only examined methanol poisoning [5]. Furthermore, they stated that the dialysis rate elimination constant for the toxin would need to be predetermined for any particular dialysis regimen. If this was not available, they suggested that at least three intradialytic measurements would be required to estimate clearance. Our experience shows that such precision is not required.

The clearance of alcohols by hemodialysis is predictable and may be easily estimated. Such an approach requires only knowledge of blood pump speed, dialyzer urea clearance, initial toxin concentration, and Watson estimate of total body water. Therapy may then be planned and initiated with minimal laboratory workload.

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